SEQUENCE LISTING

<110> Emil D. Kakkis Becky Tanamachi JUL 2 4 2002 &

RECEIVED

JUL 3 1 2002

TECH CENTER 1600/2900

<120> Recombinant Alpha-L-Iduronidase, Methods for Producing and Purifying the Same and Methods for Treating Diseases Caused by Deficiencies Thereof

```
<130> 08000051US00
```

<140> 09/439,923 <141> 1999-11-12

<160>(2)

<170> FastSEQ for Windows Version 3.0

<210> 1

<211> 6200

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1558)...(3516)

<400> 1

gacggatcgg gagatctccc gatcccctat ggtcgactct cagtacaatc tgctctgatg 60 ccgcatagtt aagccagtat ctgctccctg cttgtgtgtt ggaggtcgct gagtagtgcg 120 cgagcaaaat ttaagctaca acaaggcaag gcttgaccga caattgcatg aagaatctgc 180 ttagggttag gcgttttgcg ctgcttcgcg atgtacgggc cagatatacg cgttgacatt 240 gattattgac tagttattaa tagtaatcaa ttacggggtc attagttcat agcccatata 300 tggagttccg cgttacataa cttacggtaa atggcccgcc tggctgaccg cccaacgacc 360 cccgcccatt gacgtcaata atgacgtatg ttcccatagt aacgccaata gggactttcc 420 attgacgtca atgggtggac tatttacggt aaactgccca cttggcagta catcaagtgt 480 atcatatgcc aagtacgccc cctattgacg tcaatgacgg taaatggccc gcctggcatt 540 atgcccagta catgacctta tgggactttc ctacttggca gtacatctac gtattagtca 600 tcgctattac catggtgatg cggttttggc agtacatcaa tgggcgtgga tagcggtttg 660 actcacgggg atttccaagt ctccacccca ttgacgtcaa tgggagtttg ttttggcacc 720 aaaatcaacg ggactttcca aaatgtcgta acaactccgc cccattgacg caaatgggcg 780 gtaggcgtgt acggtgggag gtctatataa gcagagctct ctggctaact agagaaccca 840 ctgcttaact ggcttatcga aattaatacg actcactata gggagaccca agcttcgcag 900 aatteetgeg getgetaeag tgtgteeage gteetgeetg getgtgetga gegetggaae 960 agtggcgcat cattcaagtg cacagttacc catcctgagt ctggcacctt aactggcaca 1020 attgccaaag tcacaggtga gctcagatgc ataccaggac attgtatgac gttccctgct 1080 cacatgeetg etttetteet ataatacaga tggtcaacta actgeteatg teettatate 1140 acagagggaa attggagcta tctgaggaac tgcccagaag ggaagggcag aggggtcttg 1200 ctctccttgt ctgagccata actcttcttt ctaccttcca gtgaacacct tcccacccca 1260 ggtccacctg ctaccgccgc cgtcggagga gctggccctg aatgagctct tgtccctgac 1320 atgcctggtg cgagctttca accctaaaga agtgctggtg cgatggctgc atggaaatga 1380 ggagctgtcc ccagaaagct acctagtgtt tgagccccta aaggagccag gcgagggagc 1440 caccacctac ctggtgacaa gcgtgttgcg tgtatcagct gaaagcttga tatcgaattc 1500 cggaggcgga accggcagtg cagcccgaag ccccgcagtc cccgagcacg cgtggcc atg 1560 Met

1608



cto	gco Ala	gcg Ala 20	Pro	ccç Pro	gtg Val	gcc Ala	ccg Pro 25) Ala	gag Glu	gcc Ala	ccg Pro	g cac His	Let	g gtg Val	g cat . His	1656
gt <u>c</u> Val	gac Asp 35) Ala	gcc Ala	cgc Arg	gcg Ala	ctg Leu 40	Trp	ccc Pro	ctg Leu	cgg Arg	cgc Arg 45	, Phe	tgg Trp	agg Arg	g agc g Ser	1704
aca Thr 50	Gly	tto Phe	tgc Cys	ccc	ccg Pro 55	Leu	cca Pro	cac His	agc Ser	cag Gln 60	. Ala	gac Asp	cag Gln	tac Tyr	gtc Val 65	1752
ctc Leu	agc Ser	tgg Trp	gac Asp	cag Gln 70	Gln	ctc Leu	aac Asn	ctc Leu	gcc Ala 75	tat Tyr	gtg Val	ggc	gcc Ala	gtc Val 80	cct Pro	1800
cac His	cgc Arg	ggc Gly	atc Ile 85	aag Lys	cag Gln	gtc Val	cgg Arg	acc Thr 90	His	tgg Trp	ctg Leu	ctg Leu	gag Glu 95	ctt Leu	gtc Val	1848
acc Thr	acc Thr	agg Arg 100	Gly aaa	tcc Ser	act Thr	gga Gly	cgg Arg 105	ggc	ctg Leu	agc Ser	tac Tyr	aac Asn 110	ttc Phe	acc Thr	cac His	1896
ctg Leu	gac Asp 115	ggg Gly	tac Tyr	ctg Leu	gac Asp	ctt Leu 120	ctc Leu	agg Arg	gag Glu	aac Asn	cag Gln 125	ctc Leu	ctc Leu	cca Pro	gly 999	1944
ttt Phe 130	gag Glu	ctg Leu	atg Met	ggc Gly	agc Ser 135	gcc Ala	tcg Ser	ggc Gly	cac His	ttc Phe 140	act Thr	gac Asp	ttt Phe	gag Glu	gac Asp 145	1992
aag Lys	cag Gln	cag Gln	gtg Val	ttt Phe 150	gag Glu	tgg Trp	aag Lys	gac Asp	ttg Leu 155	gtc Val	tcc Ser	agc Ser	ctg Leu	gcc Ala 160	agg Arg	2040
aga Arg	tac Tyr	Ile	ggt Gly 165	Arg	tac Tyr	gga Gly	Leu	gcg Ala 170	cat His	gtt Val	tcc Ser	aag Lys	tgg Trp 175	aac Asn	ttc Phe	2088
gag Glu	acg Thr	tgg Trp 180	aat Asn	gag Glu	cca Pro	gac Asp	cac His 185	cac His	gac Asp	ttt Phe	gac Asp	aac Asn 190	gtc Val	tcc Ser	atg Met	2136
acc Thr	atg Met 195	caa Gln	ggc Gly	ttc Phe	ctg Leu	aac Asn 200	tac Tyr	tac Tyr	gat Asp	gcc Ala	tgc Cys 205	tcg Ser	gag Glu	ggt Gly	ctg Leu	2184
cgc Arg 210	gcc Ala	gcc Ala	agc Ser	ccc Pro	gcc Ala 215	ctg Leu	cgg Arg	ctg Leu	gga Gly	ggc Gly 220	ccc Pro	ggc Gly	gac Asp	tcc Ser	ttc Phe 225	2232
cac His	agg Arg	cca Pro	Pro	cga Arg 230	tcc Ser	ccg Pro	ctg Leu	Ser	tgg Trp 235	ggc Gly	ctc Leu	ctg Leu	cgc Arg	cac His 240	tgc Cys	2280
cac His	gac Asp	GIY	acc Thr 245	aac Asn	ttc Phe	ttc Phe	Thr	999 Gly 250	gag Glu	gcg Ala	ggc Gly	gtg Val	cgg Arg 255	ctg Leu	gac Asp	2328

Ont Cont

tac Tyr	c ato	c tco Sei 260	r Lei	c cad	c ago	g aag	ggt Gly 265	/ Ala	g cgo a Arg	c ago g Ser	tc: Se:	c ato r Ile 270	e Sei	c ato	c ctg e Leu	2376
gag Glu	g cag Glr 275	ı Glı	g aag 1 Lys	g gto Val	gto Val	gcg Ala 280	Gln	g cag Glr	g ato	c cgg Arg	g cag g Glr 285	ı Lei	tto Phe	ccc Pro	aag Lys	2424
tto Phe 290	ATS	gad Asp	acc Thr	ccc Pro	att Ile 295	Tyr	aac Asn	gac Asp	gag Glu	gcg Ala 300	Asp	c ccc	g ctg Lev	gtg Val	ggc Gly 305	2472
tgg Trp	tcc Ser	ctg Leu	g cca L Pro	cag Gln 310	Pro	tgg Trp	agg Arg	gcg Ala	gac Asp 315	Val	acc Thr	tac Tyr	gcg Ala	gcc Ala 320	atg Met	2520
gtg Val	gtg Val	aag Lys	y gtc Val 325	Ile	gcg Ala	cag Gln	cat His	cag Gln 330	Asn	ctg Leu	cta Leu	ctg Leu	gcc Ala 335	Asn	acc Thr	2568
acc Thr	tcc Ser	gcc Ala 340	Phe	ccc Pro	tac Tyr	gcg Ala	ctc Leu 345	ctg Leu	agc Ser	aac Asn	gac Asp	aat Asn 350	Ala	ttc Phe	ctg Leu	2616
agc Ser	tac Tyr 355	cac His	ccg Pro	cac His	ccc Pro	ttc Phe 360	gcg Ala	cag Gln	cgc Arg	acg Thr	ctc Leu 365	Thr	gcg Ala	cgc Arg	ttc Phe	2664
cag Gln 370	gtc Val	aac Asn	aac Asn	acc Thr	cgc Arg 375	ccg Pro	ccg Pro	cac His	gtg Val	cag Gln 380	ctg Leu	ttg Leu	cgc Arg	aag Lys	ccg Pro 385	2712
gtg Val	ctc Leu	acg Thr	gcc Ala	atg Met 390	glà aaa	ctg Leu	ctg Leu	gcg Ala	ctg Leu 395	ctg Leu	gat Asp	gag Glu	gag Glu	cag Gln 400	ctc Leu	2760
Trp	Ala	Glu	Val 405	Ser	Gln	gcc Ala	Gly	Thr 410	Val	Leu	Asp	Ser	Asn 415	His	Thr	2808
vai	GIY	Va1 420	Leu	Ala	Ser	gcc Ala	His 425	Arg	Pro	Gln	Gly	Pro 430	Ala	Asp	Ala	2856
Trp	Arg 435	Ala	Ala	Val	Leu	atc Ile 440	Tyr	Ala	Ser	Asp	Asp 445	Thr	Arg	Ala	His	2904
450	Asn	Arg	Ser	Val	Ala 455	gtg Val	Thr	Leu	Arg	Leu 460	Arg	Gly	Val	Pro	Pro 465	2952
GIÀ	Pro	GTÀ	Leu	Val 470	Tyr	gtc Val	Thr	Arg	Tyr 475	Leu	Asp	Asn	Gly	Leu 480	Cys	3000
agc Ser	ccc Pro	gac Asp	ggc Gly 485	gag Glu	tgg Trp	cgg Arg	Arg	ctg Leu 490	ggc Gly	cgg Arg	ccc Pro	Val	ttc Phe 495	ccc Pro	acg Thr	3048

gca gag cag tt Ala Glu Gln Ph 500	tc cgg cgc atg ne Arg Arg Met	g cgc gcg gct : Arg Ala Ala 505	gag gac ccg Glu Asp Pro 510	gtg gcc gcg Val Ala Ala	3096
gcg ccc cgc cc Ala Pro Arg Pi 515	cc tta ccc gcc ro Leu Pro Ala 520	a Gly Gly Arg	ctg acg ctg Leu Thr Leu 525	cgc ccc gcg Arg Pro Ala	3144
ctg cgg ctg cc Leu Arg Leu Pr 530	eg teg ett tte co Ser Leu Leu 535	g ctg gtg cac 1 Leu Val His	gtg tgt gcg Val Cys Ala 540	cgc ccc gag Arg Pro Glu 545	3192
aag ccg ccc gg Lys Pro Pro Gl	gg cag gtc acc ly Gln Val Thr 550	g cgg ctc cgc Arg Leu Arg 555	gcc ctg ccc Ala Leu Pro	ctg acc caa Leu Thr Gln 560	3240
ggg cag ctg gt Gly Gln Leu Va 56	ıl Leu Val Trp	tcg gat gaa Ser Asp Glu 570	His Val Gly	tcc aag tgc Ser Lys Cys 575	3288
ctg tgg aca ta Leu Trp Thr Ty 580	c gag atc cag r Glu Ile Gln	ttc tct cag Phe Ser Gln 585	gac ggt aag g Asp Gly Lys 5	gcg tac acc Ala Tyr Thr	3336
ccg gtc agc ag Pro Val Ser Ar 595	g aag cca tcg g Lys Pro Ser 600	Thr Phe Asn	ctc ttt gtg 1 Leu Phe Val 1 605	ctc agc cca Phe Ser Pro	3384
gac aca ggt gc Asp Thr Gly Al 610	t gtc tct ggc a Val Ser Gly 615	tcc tac cga Ser Tyr Arg	gtt cga gcc (Val Arg Ala 1 620	ctg gac tac Leu Asp Tyr 625	3432
tgg gcc cga cc Trp Ala Arg Pr	a ggc ccc ttc o Gly Pro Phe 630	tcg gac cct Ser Asp Pro 635	gtg ccg tac (Val Pro Tyr I	ctg gag gtc Leu Glu Val 640	3480
cct gtg cca ag Pro Val Pro Ar 64	g Gly Pro Pro	tcc ccg ggc Ser Pro Gly 650	aat cca tgago Asn Pro	ectgtg	3526
ctgagcccca gtg	gattaca cotoo	accoo cantcao	caa actaaaact	a asatataaa	2506
atgctgccct ccc	atcaccc ccttt	gcaat atatttt	tat attttaaaa	a aaaaaaaaaa	3586 3646
aaaaaaaaa aaa	aaaaaaa aaaaa	aaaaa aaaaaaa	aaa aaaaaaaa	a aaagaattcc	3706
tgcagcccgg ggg	atccact agttc	tagag ggcccgt	tta aacccgctc	a tcaqcctcqa	3766
ctgtgccttc tag	ttgccag ccatc	tgttg tttgccc	ctc ccccgtgcc	t tccttgaccc	3826
tggaaggtgc cact	teccaet greer	ttoot aataaaa	tga ggaaattgo	a tcgcattgtc	3886
tgagtaggtg tca gggaagacaa tag	caggeat getgg	aata caataaa	yua ygacagcaa ctc tatoootto	y ggggaggatt	3946 4006
gaaccagctg ggg	ctcgaga qcttq	gogta atcatoo	tca tagchghth	c ctatatass	4006 4066
ttgttatccg ctca	acaattc cacaca	aacat acgagcc	gga agcataaaq	t gtaaaqcctq	4126
gggtgcctaa tgag	gtgagct aactca	acatt aattgcg	ttg cgctcactg	c ccgctttcca	4186
gtcgggaaac ctgt	tegtgee agetge	catta atgaatc	ggc caacgcgcg	g ggagaggcgg	4246
tttgcgtatt ggg	cgctctt ccgctt	cctc gctcact	gac tegetgege	t caatcattca	4306
getgeggega gege	grandag otdact aagaaca totoo	caaa ggcggta	ata cggttatcc	a cagaatcagg	4366
ggataacgca ggaa ggccgcgttg ctgg	acgitti tecata	agget cegecee	caa aayyccagg cct gacgaggat	a accgtaaaaa	4426 4486
acgctcaagt caga	aggtggc gaaaco	cgac aggacta	taa aqataccaq	o acaaaaateg g cgtttccccc	4486 4546
tggaagetee etge	gtgcgct ctccto	ittcc gaccctg	ccg cttaccgga	t acctgtccgc	4606
ctttctccct tcgc	ggaagcg tggcgo	ctttc tcaatgc	tca cgctgtagg	t atctcaqttc	4666
ggtgtaggtc gttc	egeteca agetge	gctg tgtgcac	gaa ccccccgtt	c agcccgaccg	4726
ctgcgcctta tccg	ygtaact atcgto	rtga gtccaac	ccg gtaagacac	g acttatcgcc	4786

actggcagca gccactggta acaggattag cagagcgagg tatgtaggcg gtgctacaga 4846 gttcttgaag tggtggccta actacggcta cactagaagg acagtatttg gtatctgcgc 4906 tctgctgaag ccagttacct tcggaaaaag agttggtagc tcttgatccg gcaaacaaac 4966 caccgctggt agcggtggtt tttttgtttg caagcagcag attacgcgca gaaaaaaagg 5026 atctcaagaa gatcctttga tcttttctac ggggtctgac gctcagtgga acgaaaactc 5086 acgttaaggg attttggtca tgagattatc aaaaaggatc ttcacctaga tccttttaaa 5146 ttaaaaaatga agttttaaat caatctaaag tatatatgag taaacttggt ctgacagtta 5206 ccaatgctta atcagtgagg cacctatctc agcgatctgt ctatttcgtt catccatagt 5266 tgcctgactc cccgtcgtgt agataactac gatacgggag ggcttaccat ctggccccag 5326 tgctgcaatg ataccgcgag acccacgctc accggctcca gatttatcag caataaacca 5386 gccagccgga agggccgagc gcagaagtgg tcctgcaact ttatccgcct ccatccagtc 5446 tattaattgt tgccgggaag ctagagtaag tagttcgcca gttaatagtt tgcgcaacgt 5506 tgttgccatt gctacaggca tcgtggtgtc acgctcgtcg tttggtatgg cttcattcag 5566 ctccggttcc caacgatcaa ggcgagttac atgatccccc atgttgtgca aaaaagcggt 5626 tagctccttc ggtcctccga tcgttgtcag aagtaagttg gccgcagtgt tatcactcat 5686 ggttatggca gcactgcata attctgttac tgtcatgcca tccgtaagat gcttttctgt 5746 gactggtgag tactcaacca agtcattctg agaatagtgt atgcggcgac cgagttgctc 5806 ttgcccggcg tcaatacggg ataataccgc gccacatagc agaactttaa aagtgctcat 5866 cattggaaaa cgttcttcgg ggcgaaaact ctcaaggatc ttaccgctgt tgagatccag 5926 ttcgatgtaa cccactcgtg cacccaactg atcttcagca tcttttactt tcaccagcgt 5986 ttctgggtga gcaaaaacag gaaggcaaaa tgccgcaaaa aagggaataa gggcgacacg 6046 gaaatgttga atactcatac tcttcctttt tcaatattat tgaagcattt atcagggtta 6106 ttgtctcatg agcggataca tatttgaatg tatttagaaa aataaacaaa taggggttcc 6166 gcgcacattt ccccgaaaag tgccacctga cgtc 6200

<210> 2 <211> 653 <212> PRT <213> Homo sapiens

<400> 2

Met Arg Pro Leu Arg Pro Arg Ala Ala Leu Leu Ala Leu Leu Ala Ser Leu Leu Ala Ala Pro Pro Val Ala Pro Ala Glu Ala Pro His Leu Val 25 His Val Asp Ala Ala Arg Ala Leu Trp Pro Leu Arg Arg Phe Trp Arg Ser Thr Gly Phe Cys Pro Pro Leu Pro His Ser Gln Ala Asp Gln Tyr Val Leu Ser Trp Asp Gln Gln Leu Asn Leu Ala Tyr Val Gly Ala Val 75 Pro His Arg Gly Ile Lys Gln Val Arg Thr His Trp Leu Leu Glu Leu Val Thr Thr Arg Gly Ser Thr Gly Arg Gly Leu Ser Tyr Asn Phe Thr 105 His Leu Asp Gly Tyr Leu Asp Leu Leu Arg Glu Asn Gln Leu Leu Pro 120 125 Gly Phe Glu Leu Met Gly Ser Ala Ser Gly His Phe Thr Asp Phe Glu 135 Asp Lys Gln Gln Val Phe Glu Trp Lys Asp Leu Val Ser Ser Leu Ala Arg Arg Tyr Ile Gly Arg Tyr Gly Leu Ala His Val Ser Lys Trp Asn 170 Phe Glu Thr Trp Asn Glu Pro Asp His His Asp Phe Asp Asn Val Ser 185 Met Thr Met Gln Gly Phe Leu Asn Tyr Tyr Asp Ala Cys Ser Glu Gly 200 Leu Arg Ala Ala Ser Pro Ala Leu Arg Leu Gly Gly Pro Gly Asp Ser 215 220 Phe His Arg Pro Pro Arg Ser Pro Leu Ser Trp Gly Leu Leu Arg His 225 230 235 240

al conti

Cys His Asp Gly Thr Asn Phe Phe Thr Gly Glu Ala Gly Val Arg Leu 245 250 Asp Tyr Ile Ser Leu His Arg Lys Gly Ala Arg Ser Ser Ile Ser Ile 260 265 Leu Glu Gln Glu Lys Val Val Ala Gln Gln Ile Arg Gln Leu Phe Pro Lys Phe Ala Asp Thr Pro Ile Tyr Asn Asp Glu Ala Asp Pro Leu Val 295 Gly Trp Ser Leu Pro Gln Pro Trp Arg Ala Asp Val Thr Tyr Ala Ala 310 315 Met Val Val Lys Val Ile Ala Gln His Gln Asn Leu Leu Leu Ala Asn 325 330 Thr Thr Ser Ala Phe Pro Tyr Ala Leu Leu Ser Asn Asp Asn Ala Phe 340 345 Leu Ser Tyr His Pro His Pro Phe Ala Gln Arg Thr Leu Thr Ala Arg 360 Phe Gln Val Asn Asn Thr Arg Pro Pro His Val Gln Leu Leu Arg Lys 375 380 Pro Val Leu Thr Ala Met Gly Leu Leu Ala Leu Leu Asp Glu Glu Gln 390 395 Leu Trp Ala Glu Val Ser Gln Ala Gly Thr Val Leu Asp Ser Asn His 405 410 Thr Val Gly Val Leu Ala Ser Ala His Arg Pro Gln Gly Pro Ala Asp 425 Ala Trp Arg Ala Ala Val Leu Ile Tyr Ala Ser Asp Asp Thr Arg Ala 435 440 His Pro Asn Arg Ser Val Ala Val Thr Leu Arg Leu Arg Gly Val Pro Pro Gly Pro Gly Leu Val Tyr Val Thr Arg Tyr Leu Asp Asn Gly Leu 475 Cys Ser Pro Asp Gly Glu Trp Arg Arg Leu Gly Arg Pro Val Phe Pro 485 490 Thr Ala Glu Gln Phe Arg Arg Met Arg Ala Ala Glu Asp Pro Val Ala 505 Ala Ala Pro Arg Pro Leu Pro Ala Gly Gly Arg Leu Thr Leu Arg Pro 520 525 Ala Leu Arg Leu Pro Ser Leu Leu Leu Val His Val Cys Ala Arg Pro 535 540 Glu Lys Pro Pro Gly Gln Val Thr Arg Leu Arg Ala Leu Pro Leu Thr 550 Gln Gly Gln Leu Val Leu Val Trp Ser Asp Glu His Val Gly Ser Lys 570 Cys Leu Trp Thr Tyr Glu Ile Gln Phe Ser Gln Asp Gly Lys Ala Tyr 585 Thr Pro Val Ser Arg Lys Pro Ser Thr Phe Asn Leu Phe Val Phe Ser 600 Pro Asp Thr Gly Ala Val Ser Gly Ser Tyr Arg Val Arg Ala Leu Asp 615 620 Tyr Trp Ala Arg Pro Gly Pro Phe Ser Asp Pro Val Pro Tyr Leu Glu 630 Val Pro Val Pro Arg Gly Pro Pro Ser Pro Gly Asn Pro

645

Cont